

TREATMENT OF NON-GONOCOCCAL URETHRITIS*†

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It is singularly appropriate that, on the occasion of a meeting of this society in the city and port of Liverpool, we should interest ourselves in the problem of venereal diseases in the seafarer and in the attempts that have been and are being made to solve them. The seaman does not as a rule contract venereal disease at sea but on land and in a port which is not his home. By reason of his calling he is more exposed to temptation than those in any other occupation. I propose to confine my remarks here to one increasingly important disease—non-gonococcal urethritis—by no means uncommon in the seafarer.

The conquest of the venereal diseases begun in the 20th century is thought, by many, to be complete. It is true that since the advent of chemotherapy, the progress has continued at an increased pace. The discovery of Salvarsan and its derivatives marked the first great step forward in the treatment of syphilis and yet many were the disappointments ahead. Much later came the so-called "sulpha" drugs with their remarkable effect on the gonococcus and other organisms in which we are interested. Again, we were doomed to considerable disappointment as one micro-organism after another became no longer sensitive to the drugs. About 13 years ago supplies of the first of the antibiotics, namely penicillin, became available for the treatment of venereal diseases, and the gonococcus was rapidly eradicated in almost all patients suffering from gonococcal urethritis. The anxiety associated with the partial failure of the sulphonamides had been alleviated and gonorrhoea became, overnight, almost a trivial disease.

For at least 150 years a few physicians had suspected that all cases of urethritis were by no means identical and yet until the discovery of the causative organism absolute proof was not possible. Even after the discovery of the gonococcus, many still doubted that the condition of non-specific or non-gonococcal urethritis existed, and it was frequently stated that all cases were gonococcal in origin even

though the gonococcus could not be demonstrated in direct smears or in culture. The solution of this problem became very much easier after the introduction of penicillin in the treatment of gonorrhoea. There was no doubt that the gonococcus was very rapidly destroyed whenever it was present, but two important points were noted:

(1) Discharge persisted in those patients in whom the gonococcus was not demonstrated.

(2) Discharge reappeared after an interval of time in some patients who previously and undoubtedly had had gonorrhoea. The gonococcus could not be demonstrated in this secondary urethral discharge.

It is now well recognized that in such cases as those cited the correct diagnosis is non-gonococcal or non-specific urethritis. Urethritis of non-gonococcal origin is probably one of the most troublesome conditions with which venereologists have to deal to-day. I do not propose to discuss the causation of this perplexing condition. Many theories, some ingenious, have been advanced, but absolute proof so far eludes us and it is possible that there are a number of different types of urethritis.

Treatment

Such are the difficulties encountered in treating this condition that, once it was shown that penicillin was of little value, it was apparent that each new antibiotic would be tried with varying degrees of success. Harkness (1953) treated a large series of patients with various antibiotics and obtained the following cure rates: terramycin 86.5 per cent., aureomycin 63 per cent., streptomycin 39 per cent., chloramphenicol 36 per cent. A cure was also obtained with terramycin in 24 out of 31 cases which had not responded to aureomycin. Willcox (1953) confirmed these findings and stated that the three most successful drugs were terramycin, aureomycin, and chloramphenicol in that order. Lyall (1953), in a large series of patients treated with streptomycin 1.0 g. and sulphathiazole 1.5 g. four times daily for 5 days, claimed 85.4 per cent. successful results in the treatment of non-gonococcal urethritis. In a

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study of over 1,600 cases of non-gonococcal urethritis, Durel, Roiron-Ratner, Siboulet, and Sorel (1954) used with varying success different methods of treatment which ranged from local applications to the urethra (aureomycin ointment 1 per cent. and Connesse jelly 2.4 per cent. or instillation of 0.5 per cent. silver nitrate solution) to antibiotics by mouth. In a later study, Willcox (1955a) compared the results of treatment with varying dosage of terramycin and aureomycin and found them roughly comparable. This was confirmed by Gartman and Leibovitz (1955) who recommended 250 mg. of either antibiotic every 4 hrs for 1 week. While continuing his study of the various antibiotics in non-gonococcal urethritis, Willcox (1955b) found that erythromycin gave a failure rate of 33.9 per cent. whilst tetracycline was unsuccessful in 29.8 per cent. of cases. In a smaller series, spiromycin gave a failure rate of 22.2 per cent. (Willcox, 1956).

It will thus be appreciated that a specific has still to be found and yet it appears that the more recent antibiotics are the most effective in the largest number of cases. I have long felt that there are two possible objections to the use of these powerful substances:

- (1) The prohibitive cost of the drugs—by no means an unimportant point when one considers the vast numbers of patients requiring treatment.
- (2) The wisdom of using a powerful antibiotic for an illness, troublesome and annoying, but hardly dangerous to life. Could not such use lead to the development of drug resistance with perhaps serious or even disastrous results at some later period in life?

Doubtless other objections also exist.

It was, therefore, with these points in mind that I decided to undertake the present investigation into possible alternative methods of treatment and it was decided to treat three series of patients by different methods and to attempt to compare the results obtained in each series:

- (1) Erythromycin (Ilotycin) 200 mg. 6-hourly on a 24-hour basis for 5 days to a total of 4 g.
- (2) Streptomycin 1 g. together with sulphathiazole tablets 1 g. four times a day for 5 days to a total of 20 g.
- (3) Irrigation of the anterior and posterior urethra once daily for from 3 to 7 days with 1/8000 oxycyanide of mercury solution.

Results of Treatment

In all three series, cure was assumed if the patient presented no symptoms on the fifteenth day after treatment commenced, *i.e.* no urethral discharge containing pus cells, and a clear urine without any threads containing pus cells. It is appreciated that

this period of observation is rather short but it is difficult in a seaport where many patients are members of the merchant service to persuade them to remain ashore for long periods. Many assume that they are cured just as soon as visible signs of disease have abated. Nevertheless, many patients in the series under discussion were under observation for a considerably longer period than the minimum.

In all, 343 patients were treated and of this number 236 remained under observation for not less than 15 days. There was no selection of cases except that all were untreated on their first attendance at the clinic.

Method 1. Erythromycin (Ilotycin)

Treatment as previously outlined was given to 92 patients of whom seventy remained for the requisite period of observation; 42 (60 per cent.) were successful and 28 (40 per cent.) were considered to be failures. These figures compare very closely with those obtained by other workers.

Method 2. Streptomycin and Sulphathiazole

This treatment was given to 145 patients of whom 93 remained for the requisite period of observation, 71 (76 per cent.) were successful, and 22 (24 per cent.) were considered to be failures. Again, these figures compare reasonably closely with those obtained by other clinicians, although they are about 9 per cent. less successful than those quoted in Lyall's series. This may be accounted for in two ways:

- (1) The dosage of sulphathiazole was less, being 1 g. instead of 1.5 g. four times daily for 5 days.
- (2) The possible development of drug resistance in the 3 or 4 yrs between the two series of patients.

Method 3. Irrigations

Those of us who remember the pre-sulphonamide era will undoubtedly recall our efforts to treat urethral discharges with irrigations of various fluids and will remember the not inconsiderable success we obtained and, of course, the failures. It was felt, therefore, that a trial should again be given of irrigation of the urethra confined to those patients suffering from non-gonococcal urethritis. The solution used was oxycyanide of mercury in a strength of 1/8000 and the temperature of the irrigating fluid was 105°F. The normal routine procedure of washing the anterior urethra thoroughly before allowing the solution to pass into the bladder was adhered to rigidly. Irrigations were given once daily for from 3 to 7 days. In the series under review, 106 patients were treated by urethral irrigation alone and of this number 73 remained under observation for a minimum of 15 days from the commencement of treatment. Of these patients 62 (85 per cent.) were successful and eleven (15 per cent.) failed to respond to treatment and were treated by other methods. These figures compare more than favourably with, and cost only a fraction of the amount of, those obtained by any other method of treatment.

Discussion

A search has been made for a therapeutic procedure which would achieve success in the treatment of non-gonococcal urethritis, a clinical entity which is of increasing importance, the number of patients under treatment at any one time roughly corresponding to those being treated for gonorrhoea. Treatment by irrigation is cheap and easy to apply, is successful in a high proportion of patients, and will not cause drug resistance to develop. In my opinion it is more rational than the haphazard use of expensive antibiotics and is well worthy of trial, at least in the larger treatment centres. It is appreciated, however, that many of the smaller centres have nowadays few or no facilities for such treatment. Thus the pendulum has swung backwards as regards treatment, but not, I trust, as regards the results.

Nowadays, many consider that the best or most effective treatment of any complaint or disease must be of recent origin and preferably expensive; it has become fashionable to decry old and trusted remedies. The support of a careful selection of some of the older forms of treatment does not imply that one is old fashioned and out of touch with modern developments. Surely a careful blending of the best that is old with the best that is new is an ideal to be striven for. Many of the present day remedies, including the antibiotics, will in time probably be as outmoded as many of the once popular vaccines and sera.

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DISCUSSION

(1) **Dr. W. Macfarlane** (*Newcastle-upon-Tyne*) said that the treatment of non-gonococcal urethritis was a perplexing one. He favoured terramycin, 250 mg. administered 6-hrly for 72 hrs, the results of this treatment being usually satisfactory. He agreed entirely with Dr. Prebble that urethral irrigation produced most encouraging results, but it proved impracticable for patients other than those living in close proximity to the clinic. He was equally interested in the examination of the marital partner where the husband stoutly denied extra-marital exposure. In the majority of such cases, experience had taught him that re-infection in the husband was not rare unless husband and wife were treated simultaneously with terramycin. This applied even in those instances where the wife revealed no clinical or laboratory abnormalities. In all maritally acquired infections it was desirable, for obvious reasons, to cure the patient as quickly as possible.

(2) **Dr. W. Fowler** (*Birmingham*) said that he had studied 242 cases of non-specific urethritis of uncertain aetiology treated with potassium citrate and observed for a minimum period of 4 weeks. None of these cases presented any obvious local complications on admission and none developed other manifestations of Reiter's disease later. The rate of cure was as follows:

Week	1	2	3	4	5
Per cent. Cure ..	27·6	51·3	62·8	71·3	78·7

Dr. Fowler suggested that for the following reasons this represented a spontaneous cure-rate:

- (1) Potassium citrate was most unlikely to have any specific action.
- (2) The rapid passage of a slightly alkaline urine from the urethra during micturition could hardly be expected to have any curative action.
- (3) Although the psychological effects of the medicine could not be estimated it seemed unlikely to be significant.

As a check on these findings an independent observer examined the records of 300 cases investigated by other members of the staff and given no treatment or potassium citrate only. He found that the signs of urethritis disappeared and the urine became clear within 3 weeks in 65 per cent. of cases.

There were seventeen other cases which cleared within 21 days but relapsed 1 to 2 months later. One of these patients relapsed 12 hours after prostatic massage and 13 days later developed epididymo-orchitis. A search of the clinic records revealed that one patient out of 141 who had been treated with sulphonamides and who had been under observation for 3 or more weeks developed epididymo-orchitis. This complication also occurred in one out of 55 patients treated with penicillin plus sulphonamides. In view of these findings, Dr. Fowler asked Dr. Prebble if he thought that the rate of cure that he gave for irrigations in particular was a chance finding and of no importance in view of the lack of follow-up.

(3) **Dr. Gerald Knight** (*Birmingham*) said that the cases of trichomonas infestation must be separated from the ordinary non-specific urethritis cases, and that there were certain cases where infection was transmitted from wife to husband. Where irrigation facilities were not available the expert use of a syringe could take its place.

(4) **Dr. A. McPhater** (*Glasgow*) said that true non-specific urethritis was a relatively rare condition and that the great majority of cases seen by him had a predisposing factor. On this basis he considered a urethral discharge to be a symptom rather than a disease and that it was irrational to speak of treatment of a symptom alone. A random example would be the existence of a urethral discharge in a person with congenital abnormality of the upper urinary tract, giving a basal cystitis, and with the urethral discharge persisting after the bladder infection had cleared.